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DOI: https://doi.org/10.1016/j.clinph.2017.04.029

Association of posterior semicircular canal hypofunction on video-head-impulse testing with other vestibulo-cochlear deficits

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Short title: posterior canal hypofunction on video-head-impulse testing

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Statistics:
word count for the text (excluding figure legends, references and abstract): 3829
word count for the abstract (limit 200 words): 200
character count for the title (including spaces): 134
number of figures: 6
number of tables: 3
supplementary files: 2

Acknowledgements: The authors thank Marco Penner for technical assistance.

Funding sources for this study: None

Conflict of interest:
Dr. Tarnutzer reports no conflict of interest
Dr. Bockisch reports no conflict of interest
Mrs. Buffone reports no conflict of interest
Dr. Weber acts as an unpaid consultant and has received funding for travel from GN Otometrics.

Highlights:

- Isolated loss of the posterior canal on video-head-impulse testing is infrequent (<2%).
- Loss of the posterior canal is usually associated with additional vestibulo-cochlear impairment.
- The pattern of vestibulo-cochlear impairment depends on the underlying disease.

ABSTRACT

Objectives: The video-head-impulse test (vHIT) provides a functional assessment of all six semicircular canals (SCC). Occasionally isolated loss of the posterior canal(s) (ILPC) is diagnosed, though this finding is poorly characterized. Here we assessed how accurate that diagnosis is by measuring the co-occurrence of abnormalities on caloric irrigation, vestibular-evoked myogenic-potentials and audiometry.

Methods: We identified 52 patients with ILPC (unilateral=40, bilateral=12). We determined vHIT-gains and saccade-amplitudes and correlated vHIT-findings with other vestibulo-cochlear tests.

Results: The most frequent diagnoses were history of vestibular neuritis (13/52), Menière's disease (12/52) and vertigo/dizziness of unclear origin (13/52). Unilateral ILPC on vHIT was accompanied by a deficient horizontal canal on calorics, saccular and/or utricular deficits ipsilesionally in 33/40 (83%), while ipsilesional hearing-loss was noted in 24/40 (60%). Involvement of other sensors was highest for vestibular schwannoma (100%) and history of vestibular neuritis (92%). Bilateral deficits in ≥1 vestibulo-cochlear sensor(s) were noted in 2/12 cases with bilateral ILPC.

Conclusions: >80% of patients with unilateral ILPC had additional deficits of other parts of the vestibular organ, while this rate was ≤20% for patients with bilateral ILPC.

Significance: Dizzy patients should receive testing of the posterior canals and if abnormalities are observed, additional vestibulo-cochlear testing should be obtained.

Key words: vestibular neuritis, Menière's disease, vestibular-evoked myogenic potentials, caloric irrigation, and pure tone audiogram

INTRODUCTION

With the introduction of the video-head-impulse test (vHIT) a fast, non-invasive and quantitative assessment of all six semicircular canals (SCCs) of the vestibular organ became readily available to the clinician (Macdougall et al. , 2013). In specialized dizziness clinics, the vHIT is now a routine test for patients with dizziness, vertigo or gait imbalance. Together with caloric irrigation and otolith testing (ocular vestibular-evoked myogenic potentials (oVEMPs), cervical vestibular-evoked myogenic potentials (cVEMPs) (Curthoys, 2010, Weber et al. , 2015)), the vHIT allows comprehensive mapping of peripheral-vestibular function. As a screening test for dizzy patients, the vHIT now often provides the first evidence for peripheral-vestibular deficits. Sometimes a vHIT pattern of hypofunction restricted to one or both posterior SCCs can be observed, called isolated loss of the posterior canal (ILPC). In isolation, the clinical relevance of this finding is difficult to determine. Due to the anatomical proximity and based on clinical experience, rather a continuum between isolated involvement of a single SCC and the whole labyrinth (i.e., all 3 SCCs, both macular organs and the cochlea) is expected. These observations raise the question, to which extent other parts of the labyrinth may be involved as well in patients with seemingly isolated posterior SCC hypofunction on vHIT and what the distribution of the underlying diagnoses is. Such a closer characterization may help for the diagnostic approach to these patients. From the clinician's perspective, symptoms linked to isolated failure of the posterior SCC are often vague (typical clinical signs of unilateral peripheral-vestibular loss as spontaneous nystagmus or abnormalities on clinical head-impulse testing are frequently lacking (Chihara et al. , 2012)). Cases with isolated involvement of the posterior SCC may therefore be missed or misinterpreted as of central (e.g. stroke-related) origin (Kattah et al. , 2009).

In combination with impaired cVEMPs, unilateral hypofunction of the posterior SCC is characteristic for damage to the inferior branch of the vestibular nerve (inferior vestibulopathy, IVN) (Aw et al. , 2001, Halmagyi et al. , 2002, Chihara et al. , 2012, Kim et

al. , 2012). ILPC may potentially be caused by various other peripheral-vestibular disorders including Menière's disease, labyrinthitis and labyrinthine concussion. Noteworthy, in most previous studies, a diagnosis of IVN was established based on caloric irrigation (bilaterally normal responses) and cVEMPs (being reduced on the affected side) (Monstad et al. , 2006, Zhang et al. , 2010, Chihara et al. , 2012, Kim et al. , 2012), while involvement of the posterior SCC was not addressed.

Here we aimed to analyze the pattern of peripheral-vestibular deficits in patients with either unilateral or bilateral ILPC on video-head-impulse testing and to correlate with underlying diagnoses. We therefore compared results from vHIT with those from other routine vestibulo-cochlear tests (caloric irrigation, ocular/cervical VEMPs, pure-tone audiogram). Potentially, this may provide patterns in vestibular hypofunction helpful in narrowing down the differential diagnosis in patients.

Material and methods

In this retrospective study we identified 52 patients with ILPC. The protocol was approved by the Cantonal ethics commission Zurich (KEK-ZH-2013-0468). It was in accordance with the ethical standards laid down in the Declaration of Helsinki for research involving human subjects from 1964/2013 (7^{th} revision). Since this was a retrospective database analysis, written informed consent from the participants could not be retrieved. This approach was in accordance with the approval from the ethics committee. Prior to analysis, patient records/information was anonymized and de-identified.

Vestibular testing procedure

'Standard vHIT procedure at the University Hospital Zurich (UHZ) requires 20 valid head-impulses for each canal (Macdougall et al. , 2013). SCCs are tested in pairs according to the planes of stimulation (horizontal plane, right-anterior-left-posterior (RALP) plane, left-anterior-right-posterior (LARP) plane). For video-oculography, we used commercially available video-head-impulse testing goggles (GN Otometrics, Taastrup, Denmark) with an infrared camera recording the right eye. Horizontal and vertical eye position was measured (250Hz frame rate) and head velocity was determined by three orthogonal gyroscopes. For further analysis, eye and head velocity values were calculated', as previously described (Tarnutzer et al. , 2016).

We reviewed saccular and utricular otolith function as assessed by air- or bone-conducted cVEMPs (saccular testing) and bone-conducted oVEMPs (utricular testing). VEMPs were acquired according to the standards published elsewhere (Rosengren et al. , 2010, Weber et al. , 2015). Differences in response amplitude (left vs. right) of >30% or absent responses were considered abnormal, i.e., indicating unilateral/bilateral hypofunction. This was based on normative values obtained with the same setup and derived cut-off values (defined as mean+2SD). Whenever air-conducted cVEMPs were inconclusive or negative, we

obtained bone-conducted cVEMPs and judgment was based on the findings from the latter one. In cases with air-conducted cVEMP stimulation with different sound intensities, only results from the highest intensity were used.

Bithermal (i.e., warm (44°C) and cold (30°C) water) caloric irrigation was obtained in all patients, providing slow-phase eye velocity during stimulation. 'Unilateral hypofunction was defined as a canal paresis factor of >25% with a preserved response on the healthy side (Halmagyi et al. , 1997), while for bilateral hypofunction a nystagmus with a mean peak slow-phase velocity of <5°/sec for cold- and warm-water irrigation on each side was required (Zingler et al. , 2007)', as we used previously (Tarnutzer et al. , 2016). In addition, results from pure-tone audiograms (PTA) were retrieved. We adhered to the Council on Physical Therapy - American Medical Association (CPT-AMA) guidelines for sensorineural hearing-loss (Council on Physical Therapy, 1942). Therefore, hearing loss at four frequencies (500 Hz, 1 kHz, 2 kHz, and 4 kHz) was determined and corresponding CPT-values (based on existing data taking into account the relative importance of different frequencies) were added. Total CPT values of 20% or larger were considered significant.

Patient identification and statistical analysis

All patients included here had sought medical attention because of vertigo/dizziness, gait ataxia, or hearing-loss. We searched the University Hospital Zurich vHIT database for patients with semicircular canal hypofunction that was restricted to one or both posterior canals (period: October 1st 2012 to March 21st 2016). Eighty-eight patients (out of 2904 patients) meeting these inclusion criteria were identified for evaluation.

OtosuiteV 3.0 (GN Otometrics) was used for re-analysis of the angular vestibulo-ocular reflex (aVOR)-gains of the vHIT recordings. 'The gain of the aVOR was calculated as the ratio of cumulative slow-phase eye velocity over cumulative head velocity from the onset of the head impulse to the moment when head velocity returned to zero (Macdougall et al. ,

2013). For the quantification of corrective saccades we used custom-written MATLAB (The MathWorks, Natick, MA, USA) routines, providing cumulative overt saccade amplitudes (see (Weber et al. , 2009) for details)', as previously described (Tarnutzer et al. , 2016). Either a reduction in the gain of the aVOR or the occurrence of compensatory saccades was required to rate a given SCC as hypofunctional. have been proposed by The manufacturer of the video-goggles used (GN Otometrics) proposed cut-off values in aVOR-gain for the horizontal (0.8) and the vertical (0.7) canals. These values were in agreement with normative values for a wide range of ages reported (McGarvie et al. , 2015b). Recently proposed cut-off values suggest that saccade amplitudes above 0.7 to 0.8°/trial indicate loss of function of the canal tested (MacDougall et al. , 2016, Tarnutzer et al. , 2016). Here we adhered to the cut-off value (0.73°/trial) proposed by (Tarnutzer et al. , 2016) as the same statistical approach was used.

All vHIT traces were independently reviewed by two neuro-otologists with extensive experience (AAT, KPW). Inter-rater agreement for individual canal function (normal vs. pathological) was 0.84 (Cohen's kappa) (Cohen, 1960). Traces were evaluated for reduced aVOR-gain, increased corrective saccades or a combination of both (Tarnutzer et al. , 2016). Discordant ratings were resolved by discussion amongst the two reviewers. Twelve patients were excluded because of more extensive peripheral-vestibular hypofunction on vHIT and 24 patients were excluded since audio-vestibular testing was incomplete. ILPC was confirmed in 52 cases. The patients' medical files were searched to retrieve the most likely diagnosis related to the ILPC along with any potential diagnosis of benign paroxysmal positional vertigo (BPPV). Menière's disease was diagnosed according to the AAO-HNS 1995 guidelines (1995). The diagnosis of vestibular neuritis was based on clinical grounds (defined as a single episode with acute-onset, prolonged vertigo or dizziness and spontaneous nystagmus) as documented in the patient's medical records and – if available – on vestibular testing in the acute stage. MR-imaging was required to confirm vestibular schwannoma.

We used the generalized linear model (GLM) implemented in SPSS 22 (IBM, Armonk, NY, USA) for statistical analysis and applied Fisher's least significant difference (LSD) method to compensate for multiple comparisons. Note that we kept the level of significance always at a p-value of 0.05.

Results

Fifty-two cases with unilateral (n=40) or bilateral (n=12) ILPC were included (22 females, 59.5±15.4 years old, mean±1 standard deviation (SD). From the 12 bilateral cases, five were previously reported in a different study (Tarnutzer et al. 2016). The most frequent causes of unilateral ILPC were past medical history of VN (13/40, 33%), Menière's disease (10/40, 25%) and vestibular schwannoma (7/40, 18%) (Table 1 and supplementary file 1). In case of bilateral ILPC, the diagnosis remained unclear in the majority of cases (7/12, 58%). A typical example of left-sided ILPC due to vestibular schwannoma is shown in Figure 1.

/* Figure 1 about here */

vHIT - gains and cumulative saccade amplitudes

Gain values are shown separately for cases with left-sided (Fig. 2A, n=24), right-sided (Fig 2B, n=16) and bilateral (Fig. 2C, n=12) ILPC. While for the anterior and horizontal gains were well above the cut-off, they were decreased (i.e., below the cut-off of 0.7) for the ipsilesional posterior SCC. Likewise, cumulative saccade amplitudes were increased for all three subgroups (Fig 2, panels D-F) for the affected posterior SCC(s), being clearly above the predefined cut-off of 0.73°/trial.

/* Figure 2 about here */

We did not identify an effect of the underlying diagnosis on the average gain (df=4, Wald chi-square=3.768, p=0.438; generalized linear model) or cumulative saccade amplitude (df=4, Wald chi-square=4.386, p=0.356) of the affected posterior SCC(s).

214 **Caloric irrigation in unilateral and bilateral ILPC**

215 Ipsilesional responses to caloric irrigation were impaired (i.e., asymmetry ratio >25%)
216 in 26/40 cases (65%; asymmetry ratio=65±15% (mean±1SD)) with unilateral ILPC (Fig. 3).
217 In three unilateral cases caloric irrigation showed impairment on the side opposite to the
218 ILPC. From the 12 cases with bilateral ILPC on vHIT, caloric irrigation was bilaterally absent
219 in 1 (8%) and unilaterally impaired in 4 (33%) (supplementary file 2). Amongst the different
220 diagnoses, the rate of ipsilesional impairment on caloric irrigation varied considerably, being
221 highest for vestibular schwannoma (6/7), past medical history of VN (9/13) and various
222 causes (4/4) (Table 2).

223

224 /* Figure 3 about here */

225

226 **oVEMPs and cVEMPs**

227 oVEMPs were ipsilesionally abnormal (i.e., asymmetry ratio >30%) in 20/40 cases
228 (50%; asymmetry ratio=60±23%) with unilateral ILPC (Fig. 4). This included six cases with
229 bilaterally absent responses on oVEMPs. Significant contralesional impairment was noted in
230 one case. In patients with bilateral ILPC, no cases with bilaterally absent oVEMPs were
231 noted, while oVEMPs were unilaterally impaired in two cases (supplementary file 2). Rates of
232 ipsilesional utricular involvement were highest for vestibular schwannoma (7/7), past medical
233 history of VN (7/13) and various causes (2/4), while being infrequent in Menière's disease
234 and unclear (unilateral/bilateral) cases (Tables 2 and 3).

235 Significant ipsilesional impairment of cVEMPs (i.e., asymmetry ratio >30%) was
236 noted in 16/40 cases (40%; asymmetry ratio=72±29%) with unilateral ILPC (Figure 5). For
237 bilateral cases, both unilaterally reduced (3/12) and bilaterally absent (1/12) cVEMPs were
238 noted (supplementary file 2). Amongst the different diagnoses, the fraction of saccular

involvement on the side of ILPC was highest for vestibular schwannoma (6/7) and past medical history of VN (7/13).

/* Figures 4 and 5 about here */

Pure tone audiogram

Significant hearing-loss was identified in 32/52 cases (see supplementary file 2). While hearing-loss was restricted to the side with ILPC in 18/40 (45%) unilateral cases, it was bilateral in 6/40 (15%) patients. Amongst patients with bilateral ILPC, hearing-loss was unilateral in five patients and bilateral in one patient.

Extent of additional vestibulo-cochlear lesions

Involvement of at least one additional part of the vestibular organ ipsilesional was noted in 33/40 cases with unilateral ILPC (83%) (Table 2). Bilateral involvement of at least one vestibular sensor was found in 2/12 (17%) cases with bilateral ILPC. A lesion pattern consistent with ipsilesional involvement of the superior branch of the vestibular nerve (impaired oVEMPs and caloric irrigation) was found in 15/40 cases (38%) with unilateral ILPC. None of the cases with bilateral ILPC presented with such a pattern bilaterally.

A lesion pattern consistent with ipsilesional involvement of the inferior branch of the vestibular nerve (impaired cVEMPs and hearing-loss) was noted in 14/40 (35%) cases with unilateral ILPC, while none of the cases with bilateral ILPC presented with such a pattern bilaterally. Loss of function on all vestibulo-cochlear tests (caloric irrigation, oVEMPs, cVEMPs, pure-tone audiometry) ipsilesionally was found in 8 cases with unilateral ILPC (past medical history of VN=3; schwannoma=5), while completely normal audio-vestibular was noted in 4/52 cases (8%).

In cases with unilateral ILPC, the number of affected sensors ipsilesionally depended on the diagnosis, being higher for vestibular schwannoma than for all other diagnoses ($p \leq 0.006$, generalized linear model) (Fig. 6). While all sensors were affected with a similar frequency for the vestibular schwannoma cases, cochlear loss of function was most frequent in Menière's disease and impairment of the horizontal SCC on caloric irrigation in past medical history of VN and various diagnoses.

/* Figure 6 about here */

Benign paroxysmal positional vertigo (BPPV) in ILPC

With partial impairment of the SCCs and the otolith organs, risk for BPPV is increased (Karlberg et al. , 2000). In our cohort three patients with unilateral ILPC had posterior-canal BPPV ipsilesionally and one patient with bilateral ILPC had posterior-canal BPPV unilaterally. In two patients BPPV was reported on the healthy side. Diagnoses amongst these six patients were past medical history of VN (n=1), various (history of traumatic brain injury (n=2)), Menière's disease (n=1) and unclear unilateral (n=1) or bilateral (n=1) causes.

Discussion

Based on the video-head-impulse test, we identified isolated unilateral or bilateral hypofunction of the posterior SCCs in 52 out of 2904 patients (1.8%), making it an infrequent, but regular finding. However, more extensive vestibular testing revealed additional ipsilesional peripheral-vestibular deficits in 83% of patients with unilateral ILPC. In those patients with bilateral ILPC, additional peripheral-vestibular deficits were rarely bilateral (17%), but more often unilateral (42%). These findings suggest that truly isolated posterior SCC-loss is rather the exception than the rule and emphasizes the need for more extensive vestibulo-cochlear testing in these patients. The pattern of involvement of other vestibulo-cochlear sensors was diagnosis-dependent, being most widespread in patients with past medical history of VN and vestibular schwannoma. This was in contrast to patients with ILPC of unclear origin, showing less vestibulo-cochlear involvement, guiding to a different diagnosis.

Our case series included one patient with bilateral ILPC and a history of brainstem encephalitis. Damage to the medial longitudinal fasciculus (MLF) on both sides may explain the ILPC in this patient, as previously described by Cremer and co-workers in patients with multiple scleroris and internuclear ophthalmoplegia (Cremer et al. , 1999).

Patterns of peripheral vestibulo-cochlear hypofunction in ILPC

While all our patients were selected based on a normal horizontal video-head-impulse test, nonetheless most showed abnormal caloric responses (ipsilesional impairment in 65% of patients with unilateral ILPC; unilateral impairment in 17% of patients with bilateral ILPC). Furthermore, unilateral ILPC was accompanied by ipsilesional loss of other vestibulo-cochlear sensors supplied by the inferior branch (hearing-loss and saccular hypofunction) in only 35% of cases. This suggests that either in the majority of cases the underlying

pathomechanism was not damage to the inferior branch of the vestibular nerve (or the vestibular artery) or that damage within this branch was only partial.

Past medical history of VN

Since VN is related to damage of the vestibular nerve or its branches, the typical pattern of vestibular hypofunction can be predicted (Curthoys 2009). As the posterior SCC is innervated by the inferior branch, additional deficits of the sacculus are expected. From the 13 cases with past medical history of VN, additional hypofunction of at least one vestibular sensor innervated by the superior branch was noted in ten (77%). This suggests that these cases likely had involvement of both branches ("combined VN"), while only three cases showed damage restricted to sensors supplied by the inferior branch. In the medical files of seven of our patients with past medical history of VN we found results from previous quantitative head-impulse-testing, being recorded within days after symptom-onset in five out of seven patients. These remote measurements demonstrated previous involvement of the superior branch (mostly the horizontal SCC) in all seven cases. This suggests that at least in these seven patients (and possibly in the other six patients with past medical history of VN as well) horizontal SCC-function had recovered while the posterior SCC remained defective. A detailed patient interview will readily identify a past medical history of VN in these cases.

Noteworthy, we cannot provide any estimates on how frequent such partial recovery after VN is, as ILPC was a prerequisite for inclusion. Previously, other studies comparing recovery after unilateral VN using vHIT and caloric irrigation demonstrated discrepancies (Mahringer et al. , 2014, Zellhuber et al. , 2014, Patel et al. , 2016). In a population of dizzy patients with unilateral hypofunction of the horizontal SCC on caloric irrigation, vHIT was abnormal in only 41% (Mahringer et al. , 2014), with numbers being highest in the acute stage and decreasing with increasing disease duration. Such discrepancies for horizontal SCC-function may be related to the fact that unlike for the (video)-head-impulse test – applying a

physiological stimulus (i.e., fast head-turns, providing bilateral stimulation) – vestibular stimulation in case of caloric irrigation is artificial (and unilateral) and lacks the high frequencies provided in the vHIT. In a recent study focusing on patients with sudden sensorineural hearing-loss and acute vertigo, posterior-canal hypofunction was found in 74% of patients, while other vestibular sensors were affected about one third of cases (Pogson et al. , 2016). Most patients in this study received a diagnosis of labyrinthitis.

Menière's disease

In bilateral Menière's disease, we have found relative sparing of the anterior canals (Tarnutzer et al. , 2016). Unlike VN, the distribution of affected vestibulo-cochlear sensors does not follow a specific pattern linked to the innervation or vascular supply in Menière's disease, allowing virtually any combination of impairment. In our Menière's disease subgroup, accompanying ipsilesional hearing-loss was the most consistent finding in cases with unilateral ILPC (90%), followed by a reduced ipsilesional response on caloric irrigation in 50%. Involvement of the otolith organs was infrequent (oVEMPs=20%; cVEMPs=30%). Dissociations between video-head-impulse testing and caloric irrigation of the horizontal SCCs have been linked to the altered anatomy of the hydropic labyrinth and subsequently reduced responses of the horizontal SCC to caloric irrigation, but not to head-impulse testing (McGarvie et al. , 2015a). This, however, does not explain the pattern of reduced posterior SCC-function with preserved anterior and horizontal canals on video-head-impulse testing.

Vestibular Schwannoma

We found seven cases of ILPC from vestibular nerve compression due to schwannoma. While for small (≤14mm diameter) schwannoma at least one (out of five) vestibular test was abnormal in 59%, this number increased to at least three abnormal tests in

86% of patients with medium-to-large schwannoma (>14mm) (Taylor et al. , 2015). Vestibular schwannoma will either originate from the superior or the inferior branch and growth and compression results in hypofunction of sensors linked to either branch in the majority of cases (58%) (Taylor et al. , 2015). Interestingly, we identified seven patients who showed sparing of the anterior and horizontal SCC on video-head-impulse testing. A dissociation between horizontal SCC-function on caloric irrigation (being impaired) and video-head-impulse testing (being preserved) was previously reported in a case series (Blodow et al. , 2015) and in a single case with intra-labyrinthine schwannoma (Machner et al. , 2007). Due to our study design, we cannot provide any data on the frequency of this pattern amongst all patients with vestibular schwannoma. Considering hypofunction on caloric irrigation and on both cVEMPs and oVEMPs in five out of seven cases, however, deficits were extensive in our cases as well, despite sparing of the anterior and horizontal canal on the vHIT.

Low rate of involvement of other vestibular sensors in unclear cases

Cases with unclear cause of unilateral/bilateral ILPC were distinct from the other subgroups in several aspects: 1) regarding leading symptoms, (episodic) gait imbalance was more frequent than vertigo or dizziness, 2) other vestibular sensors were affected in 50% or less of cases, indicating more limited vestibulo-cochlear deficits than in other subgroups, and 3) ipsilesional hearing-loss was rarely noted. Likely failure to identify a specific cause was linked to the more subtle clinical presentation and negative vestibulo-cochlear testing in these patients. On video-head-impulse testing, however, ILPC was clearly detectable in these cases and average gains and cumulative saccade amplitudes of the posterior SCC(s) were not significantly different from the other subgroups. Within the spectrum of clinical presentations of bilateral vestibular loss, those cases with bilateral ILPC may represent the mildest form

with sparing of the other SCCs. This contrasts cases with more extensive bilateral vestibular impairment such as due to inner-ear infections or gentamicin (Tarnutzer et al. , 2016).

Limitations

We used a retrospective study design and selected a subgroup of patients presenting to our clinic based on the results of a single test. We therefore cannot make any conclusions on the prevalence of ILPC compared to other patterns of peripheral-vestibular hypofunction. With a clear focus on vertigo and dizziness, auditory testing was less detailed than vestibular testing. We could therefore not retrieve more detailed information about auditory nerve function than pure tone audiograms.

While vestibular testing was standardized and all head-impulses were analyzed with the same version of the GN-Otometrics software, we did not perform a uniform clinical examination and therefore had to rely on the diagnosis as noted in the medical files. Noteworthy, all patients were seen at the interdisciplinary center for dizziness and balance disorders by specialized neuro-otologists. While for Menière's disease AAO-HNS 1995 guidelines were used routinely and MR-imaging was mandatory for cases with vestibular schwannoma, the diagnosis of vestibular neuritis was based on clinical grounds. In 13/52 patients no specific diagnosis was provided in the medical files available. Potentially, repeated and structured history taking and detailed vestibulo-cochlear testing may have resulted in a diagnosis. Furthermore, we might have missed follow-up diagnostic testing performed at another hospital, not documented in our files.

CONCLUSIONS

Overall, ILPC is an infrequent finding, representing less than 2% of all patients having received video-head-impulse testing at our institution. In patients presenting with dizziness, the posterior canals should be measured and if abnormalities are observed, more extensive vestibulo-cochlear testing should be obtained. In these patients, additional vestibular deficits can be expected in more than 80%. The pattern of vestibulo-cochlear impairment depends on the underlying disease, being highest for vestibular schwannoma and past medical history of VN.

410 **TABLES**

Table 1: *isolated loss of the posterior canal(s) on vHIT – underlying diagnoses*			
Diagnosis	**Unilateral ILPC (%)**	**Bilateral ILPC (%)**	**Total**
Hypofunction of unclear origin	6 (12)	7 (13)	13 (25)
Past medical history of VN	13 (25)	0 (0)	13 (25)
Menière's disease	10 (19)	2 (4)	12 (23)
Vestibular schwannoma	7 (13)	0 (0)	7 (13)
Possible vestibular migraine	1 (2)	1 (2)	2 (4)
History of TBI	1 (2)	1 (2)	2 (4)
Acute VN	1 (2)	0 (0)	1 (2)
Repetitive hemorrhagic labyrinthitis	1 (2)	0 (0)	1 (2)
History of brainstem encephalitis	0 (0)	1 (2)	1 (2)
All	**40 (77%)**	**12 (23%)**	**52 (100%)**

411

412 Abbreviations: ILPC=isolated loss of the posterior canal(s); TBI=traumatic brain injury; VN=vestibular neuritis.

Table 2: *extent of ipsilesional vestibulo-cochlear involvement* ***in unilateral ILPC*** *on vHIT*							
Disease	**Caloric irrigation: Impaired horizontal canal (n, %)***	**oVEMPs: Impaired utriculus (n, %)†**	**Calorics & oVEMPs: both impaired (n, %)**	**cVEMP: impaired sacculus (n, %)†**	**Impairment of any of the three (calorics, oVEMP, cVEMP) (n, %)**	**PTA: Hearing loss (CPT-AMA) (n, %)‡**	**PTA & cVEMPs: Both impaired (n, %)**
Past medical history of VN (n=13)	9, 69%	7, 53.8%	6, 46%	7, 54%	12, 92%	5, 39%	4, 31%
Menière's disease (n=10)	5, 50%	2, 20.0%	2, 20%	3, 30%	7, 70%	9, 90%	3, 30%
Schwannoma (n=7)	6, 86%	7, 100.0%	6, 87%	6, 87%	7, 100%	7, 100%	6, 87%
Unilateral ILPC of unclear origin (n=6)	2, 33%	2, 33.3%	1, 17%	0, 0%	3, 50%	1, 17%	0, 0%
Various causes (n=4)§	4, 100%	2, 50.0%	2, 50%	0, 0%	4, 100%	2, 50%	1, 25%
Total unilat. ILPC (n=40)	**26 (65%)**	**20 (50%)**	**15 (38%)**	**16 (40%)**	**33 (83%)**	**24 (60%)**	**14 (35%)**

* Impairment of the horizontal canal was considered significant if the asymmetry ratio was >25% in favor of the other side or if mean cold/warm water caloric irrigation peak slow-phase velocity on both sides was less than 5°/sec (Zingler et al. , 2007).

† Impairment of vestibular-evoked myogenic potentials was considered significant if the asymmetry ratio was >30% in favor of the opposite side or if responses were bilaterally absent.

‡ Significant hearing-loss was defined as CPT-AMA values >20%.

§ Included diagnoses are: possible vestibular migraine (n=1), history of traumatic brain injury (n=1), acute VN (n=1), repetitive hemorrhagic labyrinthitis (n=1).

Table 3: *extent of vestibulo-cochlear involvement* ***in bilateral ILPC*** *on vHIT**							
Disease	**Caloric irrigation: Impaired horizontal canal (n, %)†**	**oVEMPs: Impaired utriculus (n, %)‡**	**Calorics & oVEMPs: both impaired (n, %)**	**cVEMP: impaired sacculus (n, %)‡**	**Impairment of any of the three (calorics, oVEMP, cVEMP) (n, %)**	**PTA: Hearing loss (CPT-AMA) (n, %) §**	**PTA & cVEMPs: Both impaired (n, %)**
Menière's disease (n=2)	0 (+2), 0% (100%)	0 (+0), 0% (0%)	0 (+0), 0% (0%)	0 (+1), 0% (50%)	0 (+2), 0% (100%)	0 (+1), 0% (50%)	0 (+1), 0% (50%)
Bilateral ILPC of unclear origin (n=7)	1 (+0), 14% (0%)	0 (+1), 0% (14%)	0 (+1), 0% (14%)	1 (+2), 14% (29%)	2 (+1), 29% (14%)	1 (+3), 14% (57%)	0 (+2), 0% (29%)
Various causes (n=3)‖	0 (+2), 0% (67%)	0 (+1), 0% (33%)	0 (+1), 0% (33%)	0 (+0), 0% (0%)	0 (+2), 0% (67%)	0 (+1), 0% (33%)	0 (+0), 0% (0%)
Total bilateral ILPC (n=12)	**1 (+4), 8% (33%)**	**0 (+2), 0% (17%)**	**0 (+2), 0% (17%)**	**1 (+3), 0% (25%)**	**2 (+5), 17% (42%)**	**1 (+5), 8% (42%)**	**0 (+3), 0% (25%)**

* Cases with unilateral hypofunction but bilateral ILPC are in brackets.

† Impairment of the horizontal canal was considered significant if the asymmetry ratio was >25% in favor of the other side or if mean cold/warm water caloric irrigation mean peak slow-phase velocity on both sides was less than 5°/sec (Zingler et al. , 2007).

‡ Impairment of vestibular-evoked myogenic potentials was considered significant if the asymmetry ratio was >30% in favor of the opposite side or if responses were bilaterally absent.

§ Significant hearing-loss was defined as CPT-AMA values >20%.

‖ Included diagnoses are: possible vestibular migraine (n=1), history of traumatic brain injury (n=1) and history of brainstem encephalitis (n=1).

FIGURE LEGENDS

Figure 1:

Illustrative example of a patient with unilateral isolated loss of the left posterior SCC on video-head-impulse testing and as indicated by decreased gain (0.54) and increased covert and overt catch-up saccades (black arrow) (panel A). He was diagnosed with left-sided vestibular schwannoma (panel B: axial contrast-enhanced MR-image). Additional vestibular testing revealed ipsilesionally reduced response of the horizontal SCC on caloric irrigation (panel C; asymmetry ratio=44%) and impaired saccular (panel D; asymmetry-ratio=51%) and utricular (panel E; asymmetry ratio=47%) function. Furthermore, there was moderate left-sided sensorineural hearing-loss for frequencies above 2kHz on pure-tone audiogram (panel F).

Figure 2:

Mean (±1SD) gains (panels A-C) and cumulative saccadic amplitudes (panels D-F) of all patients (n=52) shown separately depending on the side of posterior canal hypofunction (left, right, bilateral). Gain values (from 0 to 1) and cumulative saccadic amplitudes (°/trial, from 0 to 2) are provided along the different hexagons. Cut-off values for reduced gains (<0.8 for the horizontal canals, <0.7 for the vertical canals) and for abnormally increased cumulative saccade amplitudes (>0.73°/trial) are indicated by dashed lines.

Figure 3:

Asymmetry ratios (AR; individual values and mean±1SD) for caloric irrigation are shown both for all patients with unilateral ILPC and the different diagnoses separately. Asymmetry ratios were considered significant if larger than ±25%, as indicated by the dashed vertical

lines and the light grey-shaded background. Cases were separated for each group based on the lesion pattern on caloric irrigation compared to the hypofunction identified on video-head-impulse testing. We distinguished between cases with weaker responses on caloric irrigation on the same side as the ILPC on vHIT (black symbols, AR with a positive sign, shown on the right side, and cases with weaker response on caloric irrigation on the opposite side as the ILPC (grey symbols, AR with a negative sign, shown on the left side). Note that the 12 cases with bilateral ILPC are not shown here (see Figure 4).

Figure 4:

Asymmetry ratios (AR; individual values and mean±1SD) for oVEMPs are shown for all patients with unilateral ILPC and the different underlying diagnoses separately. AR were considered significant if larger than ±30%, as indicated by the dashed vertical lines and the light grey-shaded background. Cases were separated for each group based on the lesion pattern in oVEMPs compared to the hypofunction identified on the video-head-impulse test. We distinguished between cases with weaker responses on oVEMPs on the same side as the ILPC on vHIT (black symbols, AR with a positive sign, shown on the right side,) and cases with weaker response on oVEMPs on the opposite side as the ILPC (grey symbols, AR with a negative sign, shown on the left side). Note that six patients had bilaterally absent oVEMPs (not shown). Those 12 cases with bilateral ILPC are not shown here (see supplementary file 2).

Figure 5:

Asymmetry ratios (AR; individual values and mean±1SD) for cVEMPs are shown for all patients with unilateral ILPC and the different underlying diagnoses separately. AR were considered significant if larger than ±30%, as indicated by the dashed vertical lines and the light grey-shaded background. Cases were separated for each group based on the lesion

pattern in cVEMPs compared to the hypofunction identified on the video-head-impulse test. We distinguished between cases with weaker responses on cVEMPs on the same side as the ILPC on vHIT (black symbols, AR with a positive sign, shown on the right side,) and cases with weaker response on cVEMPs on the opposite side as the ILPC (grey symbols, AR with a negative sign, shown on the left side). Note that one patient hat bilaterally absent cVEMPs (not shown). Those 12 cases with bilateral ILPC are not shown here (see supplementary file 2).

Figure 6:

Bar plot illustrating mean (±1SD) numbers of other ipsilesionally impaired vestibulo-cochlear sensors for different causes of *unilateral* ILPC (n=40). Each bar represents the relative frequency of hypofunction for the different sensors tested (hearing-loss due to cochlear loss of function, abnormal horizontal SCC on caloric irrigation, reduced saccular response on cVEMPs, reduced utricular response on oVEMPs) for a given cause in a stacked fashion (see inset for further explanations). On the right side, average values for all subjects are shown. Statistically significant differences (generalized linear model, least significant difference (LSD) for compensation of multiple tests) are indicated by an asterisk ('*'). Due to small numbers no such analysis was performed for the 12 cases with bilateral ILPC.

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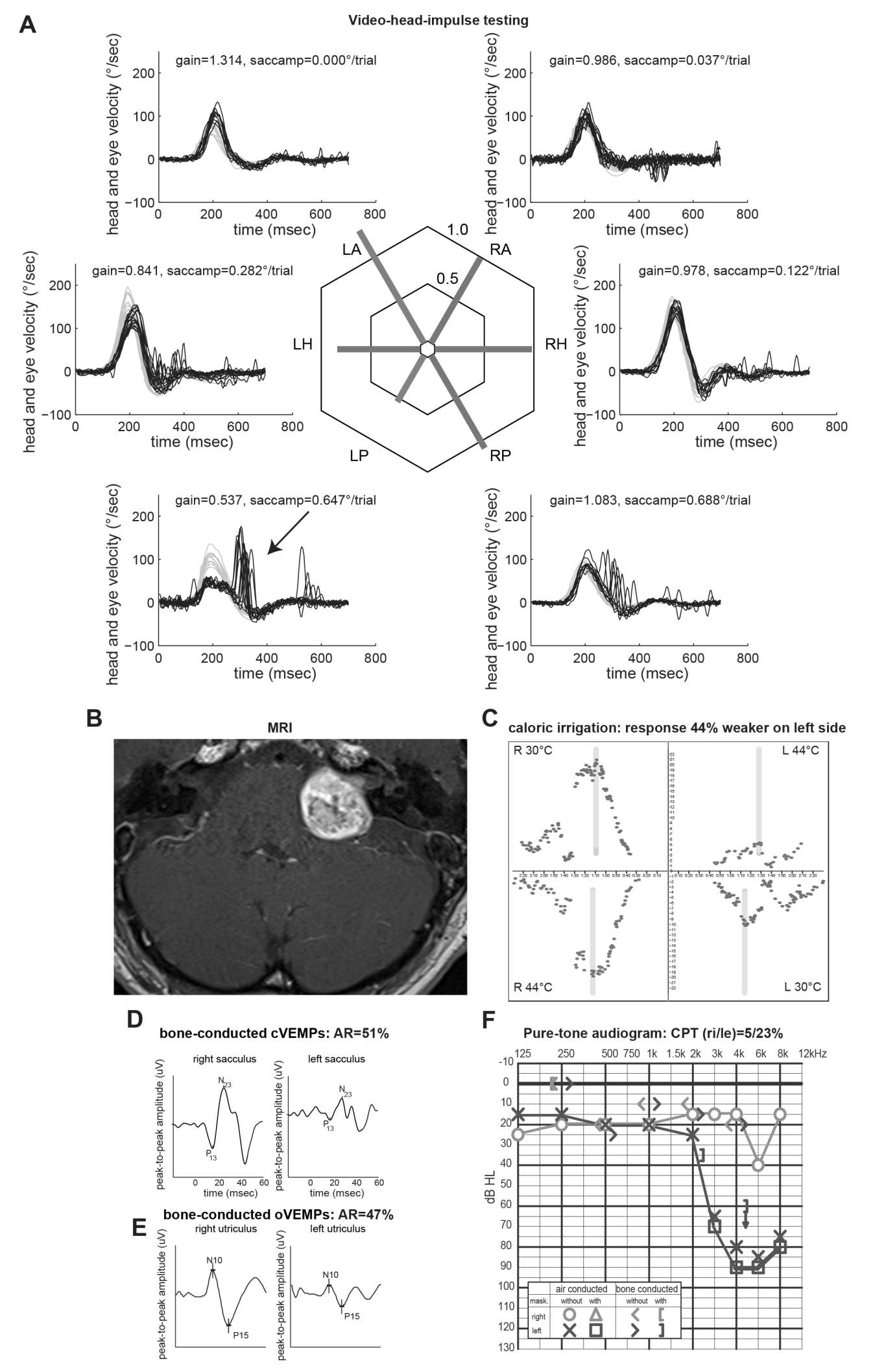
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Video-head-impulse testing
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gain=0.978, saccamp=0.122°/trial
gain=0.537, saccamp=0.647°/trial
gain=1.083, saccamp=0.688°/trial
head and eye velocity (°/sec)
time (msec)
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RH
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RP
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C
caloric irrigation: response 44% weaker on left side
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L 44°C
R 44°C
L 30°C
D
bone-conducted cVEMPs: AR=51%
right sacculus
left sacculus
peak-to-peak amplitude (uV)
time (msec)
E
bone-conducted oVEMPs: AR=47%
right utriculus
left utriculus
N10
P15
F
Pure-tone audiogram: CPT (ri/le)=5/23%
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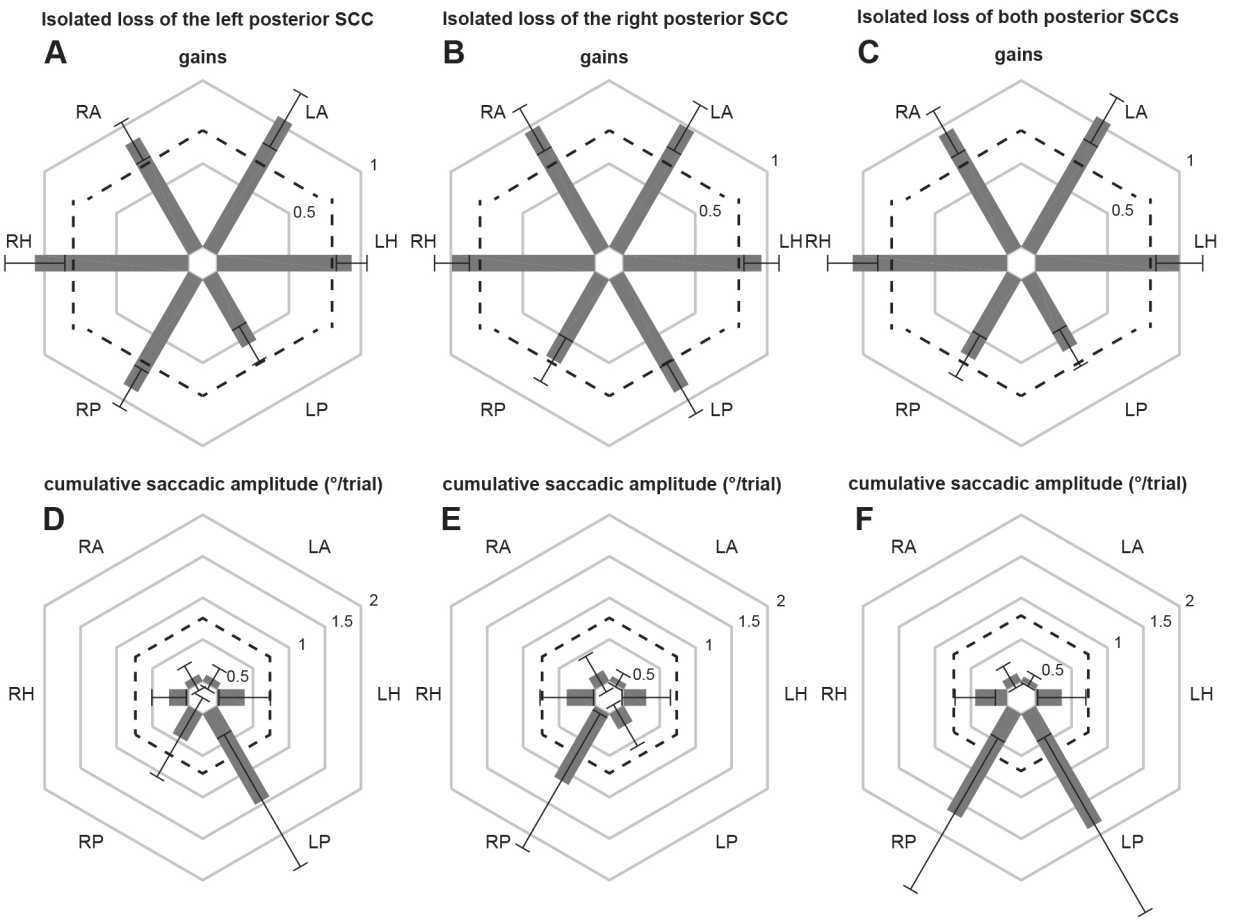
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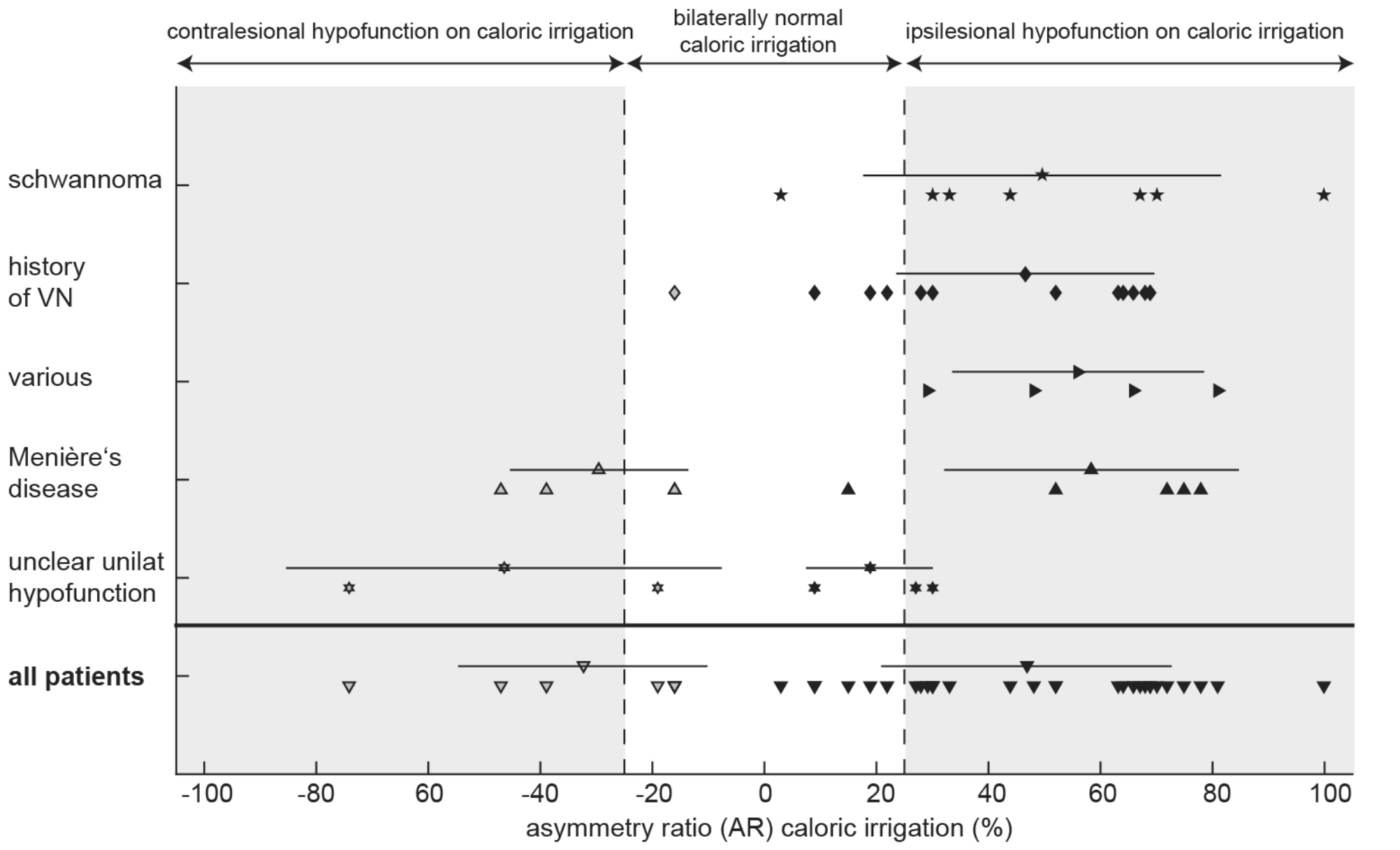
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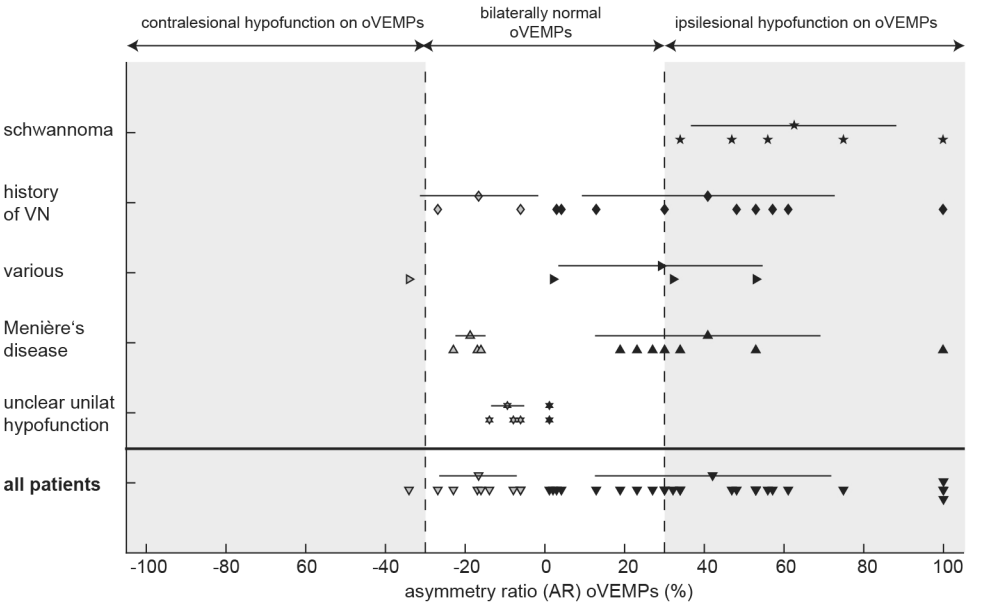
asymmetry ratio (AR) caloric irrigation (%)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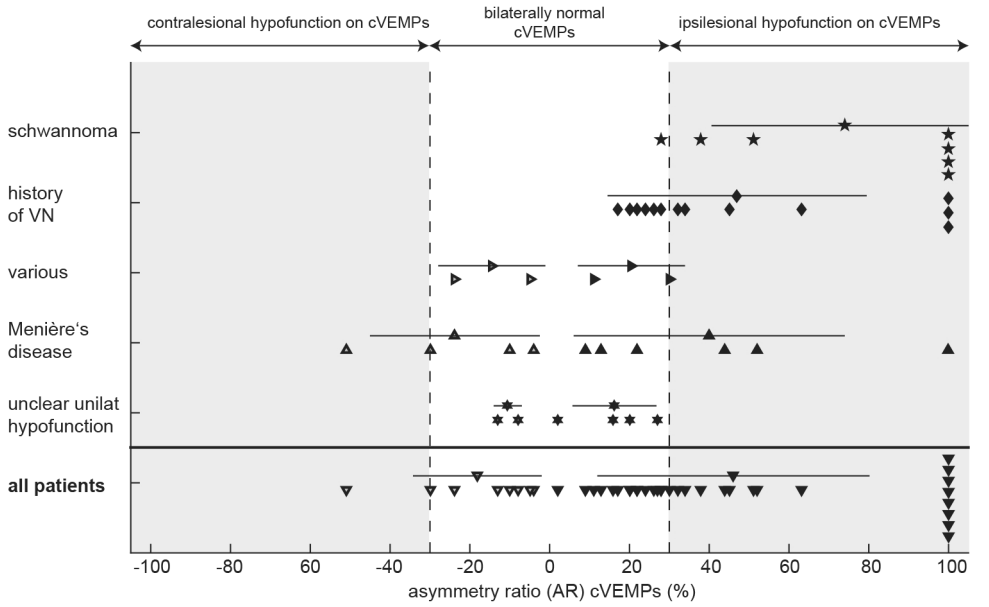
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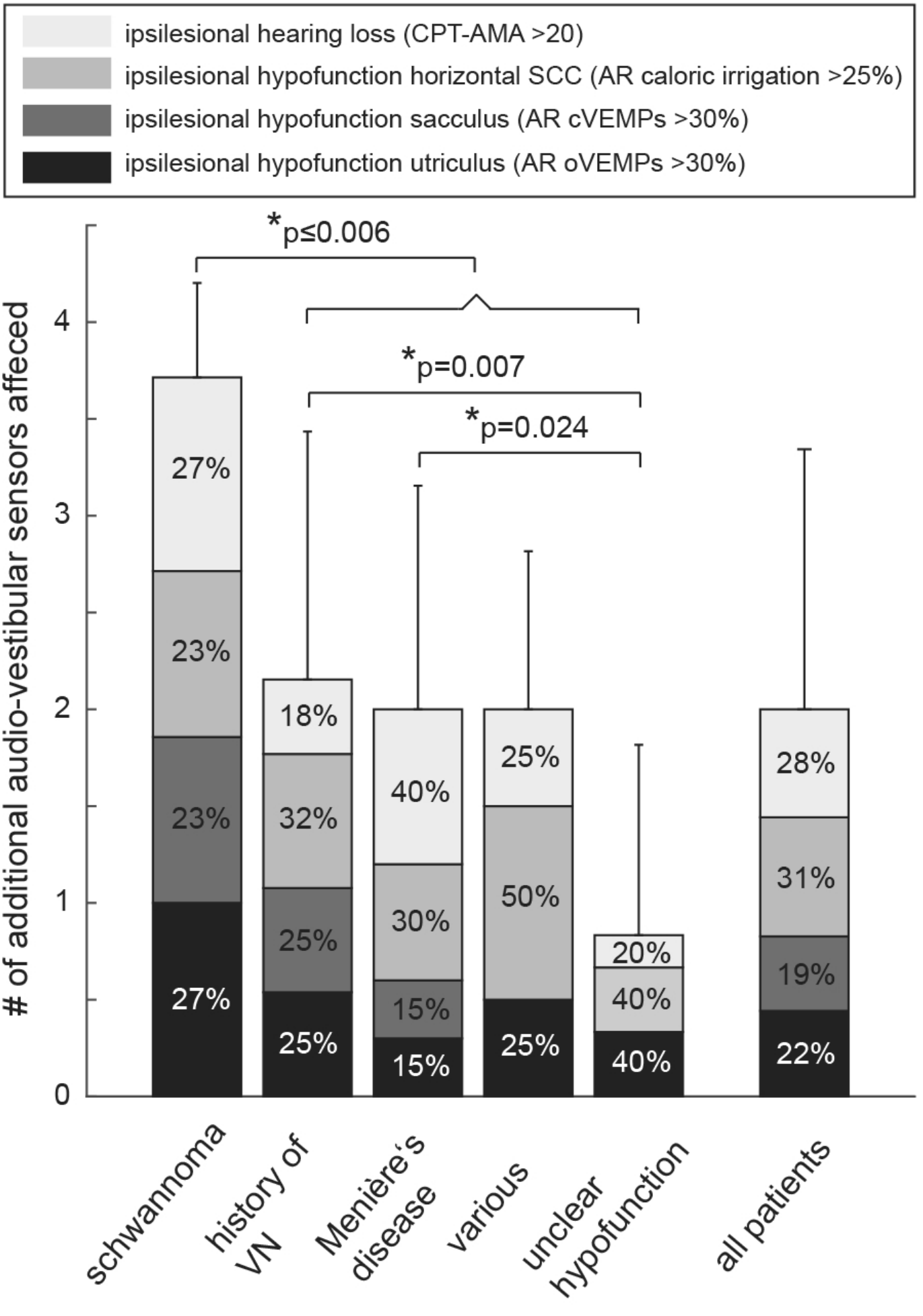
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ipsilesional hypofunction horizontal SCC (AR caloric irrigation >25%)
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*p≤0.006
*p=0.007
*p=0.024
# of additional audio-vestibular sensors affeced
0
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schwannoma
history of VN
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various
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